

DETAILED ACTION

Election/Restrictions

Applicant's election of compound of example 056 in the reply filed on October 24, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). However for the purpose of this examination the requirement for species election is withdrawn.

Status of Claims

Claims 1-19 are currently pending and are the subject of this office action.

Claims 5 and 18-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on October 24, 2007.

Claims 1-4 and 6-17 are presently under examination.

Priority

The present application is a 371 of PCT/JP04/15245 filed on 10/15/2004, which claims benefit of foreign application JAPAN 2003-357143 filed on 10/17/2003.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, and 7-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1 and 7-17 recite a composition comprising as an active ingredient a compound of formula I (see claim 1).

M.P.E.P. #2163 states: "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention....one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process".

Formula I (see claim 1) contains an R group, which can be represented among others by a (C2-C7) alkoxycarbonyl group which may be substituted with a substituent, a (C1-C13) aliphatic acyl group which may have 1 to 3 same or different substituents, an amino acid group in which the N-terminal may be protected or a 3- to 7- membered

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cyclic acyl group which may have 1 to 3 same or different substituents, or a pharmaceutically acceptable salt thereof.

Given the broad scope of the claimed subject matter, Applicant has not provided sufficient written description that would allow the skilled artisan to recognize all the substituents claimed.

Claims 1, and 7-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG v. Guardian*, 75 F.3d 1558, 1564 (Fed. Cir. 1996). As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

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- 1- the quantity of experimentation necessary,
- 2- the amount of direction or guidance provided,
- 3- the presence or absence of working examples,
- 4- the nature of the invention,
- 5- the state of the prior art,
- 6- the relative skill of those in the art,
- 7- the predictability of the art, and
- 8- the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention

The invention relates to a composition comprising as an active ingredient a compound of formula I (see claim 1).

2. The state and predictability of the art

Even though enormous progress had been made in predicting the course of a reaction, organic synthesis still remains an experimental science, since, for example, small differences in the reaction conditions (e.g. temperature, pressure, reagents, etc) can cause unpredictable outcomes. The literature is full of examples of unpredicted

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results in organic synthesis. As a few representative examples, the examiner refers to Alphonse et. al. (JACS, 2006, 128:11754-11755.) and Kwiatkowska et. al. (Chemistry of heterocyclic compounds, 2006, 42:1334-1337). Alphonse et. al, while discussing some rhodium-catalyzed stereoselective formation of Z-enamines from Allylaziridines , mention that “unexpected selectivity for the Z-isomer 2a was observed” (see page 11754, column 1, second paragraph, 4 line from the bottom). Kwiatkowska et. al. teach” unexpected results of 3-nitropropene-1 [2+3] cycloaddition to C,C,N-triphenylnitrone (see title).

3. The relative skill of those in the art

The relative skill of those in the art is generally at least that of Bachelor in Chemistry.

4. The breadth of the claims

Claims 1, and 7-17 are very broad in terms of the number of compounds claimed: formula I (see claim 1) contains an R group, which can be represented among others by a (C2-C7) alkoxycarbonyl group which may be substituted with a substituent, a (C1-C13) aliphatic acyl group which may have 1 to 3 same or different substituents, an amino acid group in which the N-terminal may be protected or a 3- to 7- membered cyclic acyl group which may have 1 to 3 same or different substituents, or a pharmaceutically acceptable salt thereof. The term substituent, without specifying what

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a substituent is, encompasses a nearly infinite an extremely divergent genus of chemical moieties.

5. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides examples for the synthesis and physical properties of approximately 60 compounds. However the specification does not provide any type of data for compounds where R is just any substituent (i.e. a substituent could be a peptide, a fatty acid, a polymer, etc). The specification provides no direction or guidance for determining the synthetic steps required to make compounds of formula I, when for example R is a polymer or hindered carboxylic acid or a hindered alkyl group.

6. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate with the scope of the claims, the skilled artisan would not accept that all the compounds of formula I with any R substituent could be made with the synthetic methods provided in the specification. How is the skilled chemist supposed to synthesize any of the numerous compounds where R is just any substituent (e.g. when the substituent is a polymer of molecular weight 5,000 or a molecule that has a very hindered carboxylic acid, or a hindered alkyl group)? Making these type of compounds would require experimentation with different synthetic routes, finding the proper reaction conditions for each synthetic step, and

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finding a method for isolating, purifying and characterizing the final compound. This is undue experimentation given the guidance and direction provided by applicants.

Accordingly, the inventions of claims 1, and 7-17 do not comply with the enablement requirement of 35 U.S.C 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation with no assurance of success.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-4 and 6 the statement: "A drug comprising" is indefinite because it is not clear if applicant is claiming "a composition comprising an active ingredient" or a "single compound that is an active ingredient".

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcos L. Sznajdman whose telephone number is 571

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270-3498. The examiner can normally be reached on Monday through Friday 9 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MLS

November 29, 2007

/Cecilia Tsang/

Supervisory Patent Examiner, Art Unit 4173